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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/405,050	09/27/99	SHOENFELD	Y ZAP-1CIPCONC

HM12/1218

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EXAMINER	
NAVARRO, A	
ART UNIT	**PAPER NUMBER**
1645	6

DATE MAILED: 12/18/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/405,050	Shoenfield et al
Examiner	**Group Art Unit**
Mark Navarro	1645

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-21 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-21 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a method of inhibiting metastasis of lymphoma in a mammal which comprises administering to the mammal a preparation of IVIG or "fragments thereof."

The specification does not adequately teach how to effectively use the claimed methods for inhibiting metastasis of lymphoma in a mammal by administering unspecified fragments of IVIG as claimed. Different types of IVIG fragments differ in their structures and biological activities. For example, fragments comprised of immunoglobulin variable regions may possess antigen-binding activity. Fc fragments may bind Fc receptors but lack antigen-binding activity. Other immunoglobulin fragments may lack any binding function (e.g., dipeptides of the claimed IVIG molecules). Given the structural and functional differences which exist among different types of immunoglobulin fragments, the type of fragments used in the claimed methods is expected to have a material bearing on whether the desired effects of inhibiting metastasis or treating primary tumors are obtained. Given that the mechanism by which IVIG inhibits metastasis of lymphomas in vivo is unknown, it is unpredictable whether the broadly recited

fragments of IVIG can be effectively used in the claimed methods. The specification exemplifies only the use of $F(ab')_2$ fragments in experimental animals. No direction or guidance are provided as to the types of fragments other than $F(ab')_2$ fragments which could be effectively administered to prevent metastases of lymphomas. It appears that undue experimentation would be required to practice the claimed methods by administering IVIG "fragments" with a reasonable expectation of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-2, 7-9, 12-13, and 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Chapel *et al.*

The claims are directed to a method of inhibiting metastasis of lymphoma in a mammal which comprises administering to the mammal a preparation of IVIG or fragments thereof.

Chapel *et al* (Clin. Res. 1988, 36(3) page 407A) disclose of patients with low grade non-Hodgkin's lymphoma receiving intravenous immunoglobulins. (See abstract).

In view that patients with lymphoma received IVIG as claimed, the result of inhibiting metastasis of the lymphoma is deemed to be an inherent result of the administered IVIG, and consequently anticipates the claimed invention.

3. Claims 1-3, 7-10, 12-14, and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Morell *et al.*

Morell *et al* (Pediatr. Infect Dis. J. Vol. 7, No. 5, pp S87-S91, 1988) disclose of 9 patients who were on cytostatic therapy for non-Hodgkin's lymphoma receiving 0.4g/kg of IVIG daily. Morell *et al* further set forth that of administering IVIG for greater than 5 consecutive days. (See page S90 and Figure 3).

In view that patients with lymphoma received IVIG in an amount of 2g/kg/month as claimed, the result of inhibiting metastasis of the lymphoma is deemed to be an inherent result of the administered IVIG, and consequently anticipates the claimed invention.

4. Claims 1-3, 6-9, 12-14, and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Besa *et al.*

Besa *et al* (American Journal of Medicine Apr. 1988, Vol. 84(4), pp 691-698) disclose of patients with Hodgkin's lymphoma and non-Hodgkin's lymphoma treated with intravenous immunoglobulin (0.4g/kg) daily for five doses followed by maintenance therapy every 21 to 28 days if evidence of recurrence was noted. (See abstract).

In view that patients with lymphoma received IVIG in an amount of 2g/kg/month as claimed, the result of inhibiting metastasis of the lymphoma is deemed to be an inherent result of the administered IVIG, and consequently anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-3, 5-14, and 16-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morell *et al* or Besa *et al* in view of Cafiero *et al*, Webb *et al* and Way.

The teachings of Morell *et al* and Besa *et al* are set forth above.

Morell *et al* and Besa *et al* do not teach of administering IVIG subcutaneously, or of a treatment modality selected from the group consisting of chemotherapy, immunotherapy, radiation therapy and surgery.

Cafiero *et al* (Surgery Vol. 112, No. 1, pp 24-31, 1992) teach of the administration of IVIG to patients before and after the surgical removal of colon tumors, which resulted in a significant decrease in postoperative infection. (See abstract).

Webb *et al* (Lancet Vol. 337, June 29, 1991, pp 1617-1618) teach of infusing intravenous immunoglobulin subcutaneously. (See page 1617).

Way (Current Surgical Diagnosis & Treatment, Ninth Edition, Norwalk, Connecticut, 1991, page 93) set forth that lymphomas are best treated with radiotherapy and combination chemotherapy. (See page 93).

In view that 1) Morell *et al* and Besa *et al* have disclosed administering 2g/kg/month of IVIG to patients with lymphomas, and that 2) Cafiero *et al* set forth that administration of IVIG both before and after removal of tumors resulted in lower postoperative infections, and that 3) Webb *et al* have taught of administering IVIG subcutaneously, and that 4) Way has taught that lymphomas are best treated with radiotherapy and combination chemotherapy, it would have been *prima facie* obvious to have treated the patients with lymphoma as set forth by Morell *et al* and Besa *et al* with radiotherapy and combination chemotherapy as taught by Way, and to further administer the IVIG subcutaneously as taught by Webb *et al* and to further administer the IVIG after the treatment in view of the teachings of Cafiero *et al*. One would have been motivated to

produce such a method in view of the teachings of Way that lymphomas are best treated with radiotherapy and combination chemotherapy, and in view of the teachings of Caifero *et al* which set forth that patients receiving IVIG after surgery had lower postoperative infections.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 5,965,130. Although the conflicting claims are not identical, they are not patentably distinct from each other because each set of claims is directed to inhibiting metastasis comprising administering IVIG.

7. Claims 1-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,562,902. Although the

conflicting claims are not identical, they are not patentably distinct from each other because each set of claims is directed to inhibiting metastasis comprising administering IVIG.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro, whose telephone number is (703) 306-3225. The examiner can be reached on Monday - Thursday from 8:00 AM - 6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Lynette Smith can be reached at (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1645 by facsimile transmission. Papers should by faxed to Group 1645 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Mark Navarro

Primary Examiner

December 11, 2000